

SUPPLEMENTAL AMENDMENT
CPA of USSN 09/429,003

The Patent Office is authorized to charge any fees necessary for the continued pendency of the above-identified application to our Deposit Account No. 19-4880.

Accordingly, please amend the above-identified application as follows.

IN THE CLAIMS:

Please cancel Claims 18-36.

Please add the following new claims:

Sub E1
-- Claim 37. A method of obtaining isolated selected mRNA species or isolated selected cDNA species useful for diagnosing or identifying a disease or condition or stage thereof in a eukaryotic organism comprising the steps of:

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- (a) isolating mRNA from cells of one or more eukaryotic organisms which are known to have said disease or condition or a stage thereof (diseased sample), wherein said cells are obtained from, and originate from, a part of said organism distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
 - (b) isolating mRNA from corresponding cells of one or more corresponding normal eukaryotic organisms (normal sample), wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
 - (c) separating, by a non-sequence based separation technique, mRNA species or cDNA species present within each of the resulting isolated mRNA or

SUPPLEMENTAL AMENDMENT
CPA of USSN 09/429,003

- isolated cDNA of step (a) and step (b), wherein the resulting separated mRNA species are optionally subject to reverse transcription to obtain separated cDNA species;
- (d) selecting two or more mRNA species or two or more cDNA species from the resulting separated mRNA species or resulting separated cDNA species obtained in step (c), respectively, which are present at a different level in the normal sample than in the diseased sample by identifying a signal corresponding to each mRNA species or cDNA species, wherein the resulting selected two or more mRNA species are optionally subjected to reverse transcription to obtain two or more selected cDNA species; and
- (e) isolating the resulting two or more selected mRNA species or resulting two or more selected cDNA species obtained in step (d) to obtain isolated selected mRNA species or isolated selected cDNA species, wherein the resulting isolated selected mRNA species are optionally subjected to reverse transcription to obtain isolated selected cDNA species.

Claim 38. The method as claimed in Claim 37, further comprising the step of:

- (f) immobilizing the resulting isolated selected mRNA species or isolated selected cDNA species of step (e) on at least one solid support.

SUPPLEMENTAL AMENDMENT
CPA of USSN 09/429,003

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67</sup> Claim 39. The method as claimed in Claim 38, wherein, prior to immobilizing in step (f), the resulting isolated selected mRNA species or isolated selected cDNA species of step (e) are amplified.

Claim 40. The method as claimed in Claim 37, wherein in steps (a) and (b), the resulting isolated mRNA is subjected to reverse transcription to obtain isolated cDNA.

Claim 41. The method as claimed in claim 40, wherein said isolated cDNA is amplified.

Claim 42. The method as claimed in Claim 41, wherein said isolated cDNA is labelled.

Claim 43. The method as claimed in Claim 37, wherein, in step (e), between 50 and 100 mRNA species or cDNA species are isolated and selected.

Claim 44. The method as claimed in Claim 37, wherein, in step (e), between 10 and 500 mRNA species or cDNA species are isolated and selected.

Claim 45. The method as claimed in Claim 37, wherein, in step (c), said separation technique is gel electrophoresis.

Claim 46. The method as claimed in Claim 37, wherein said organism is human.

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67</sup> Claim 47. The method as claimed in Claim 38, wherein said solid support is a filter.

Claim 48. The method as claimed in Claim 37, wherein said disease is cancer.

Claim 49. The method as claimed in Claim 37, wherein said cells are isolated from tissue, body fluid or body waste of said eukaryotic organism.

SUPPLEMENTAL AMENDMENT
CPA of USSN 09/429,003

Claim 50. The method as claimed in Claim 49, wherein said body fluid is blood.

Claim 51. The method as claimed in Claim 37, wherein said disease is selected from the group comprising stomach, lung, breast, prostate gland, bowel and skin cancer.

Claim 52. The method as claimed in Claim 37, wherein said disease is Alzheimer's disease.

Claim 53. A gene transcript pattern probe kit for diagnosing or identifying a disease or condition or stage thereof in a eukaryotic organism comprising at least one solid support having immobilized thereon two or more mRNA species or cDNA species isolated and selected in accordance with the method as recited in steps (a) to (e) of Claim 37, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51 or 52.

Claim 54. The gene transcript pattern probe kit as claimed in Claim 53, further comprising, for comparative purposes, mRNA or cDNA from a normal sample; or mRNA or cDNA from a diseased sample; or mRNA or cDNA from both a normal sample and a diseased sample.

Claim 55. The gene transcript pattern probe kit as claimed in Claim 53, further comprising, for comparative purposes, a standard gene transcript pattern obtained by a method comprising the steps of:

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- (a) isolating mRNA from cells of one or more eukaryotic organisms which are known to have said disease or condition or a stage thereof (diseased sample), wherein said cells are obtained from, and originate from, a part of said organism

SUPPLEMENTAL AMENDMENT
CPA of USSN 09/429,003

distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA; and

- (b) hybridizing the resulting isolated mRNA or isolated cDNA of step (a) to the isolated selected mRNA species or isolated selected cDNA species which are immobilized in the gene transcript pattern probe kit of Claim 53, and assessing the amount of hybridisation so as to obtain said standard gene transcript pattern, wherein the isolated selected mRNA species or isolated selected cDNA species are specific for said disease or condition or stage thereof.

Sub E47 Claim 56. A method of preparing a gene transcript pattern probe kit comprising the steps of:

- (a) isolating mRNA from cells of one or more eukaryotic organisms which are known to have said disease or condition or a stage thereof (diseased sample), wherein said cells are obtained from, and originate from, a part of said organism distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
- (b) isolating mRNA from corresponding cells of one or more corresponding normal eukaryotic organisms (normal sample), wherein the resulting isolated

SUPPLEMENTAL AMENDMENT
CPA of USSN 09/429,003

- mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
- (c) separating, by a non-sequence based separation technique, mRNA species or cDNA species present within each of the resulting isolated mRNA or isolated cDNA of step (a) and step (b), wherein the resulting separated mRNA species are optionally subject to reverse transcription to obtain separated cDNA species;
- (d) selecting two or more mRNA species or two or more cDNA species from the resulting separated mRNA species or resulting separated cDNA species obtained in step (c), respectively, which are present at a different level in the normal sample than in the diseased sample by identifying a signal corresponding to each mRNA species or cDNA species, wherein the resulting selected two or more mRNA species are optionally subjected to reverse transcription to obtain two or more selected cDNA species;
- (e) isolating the resulting two or more selected mRNA species or resulting two or more selected cDNA species obtained in step (d) to obtain isolated selected mRNA species or isolated selected cDNA species, wherein the resulting isolated selected mRNA species are optionally subjected to reverse transcription to obtain isolated selected cDNA species; and

SUPPLEMENTAL AMENDMENT
CPA of USSN 09/429,003

- (i) immobilizing the resulting isolated selected mRNA species or isolated selected cDNA species of step (e) on at least one solid support so as to form a gene transcript pattern probe kit.

Claim 57 A method of preparing a standard gene transcript pattern characteristic of a disease or condition or stage thereof of a eukaryotic organism comprising the steps of:

- (a) isolating mRNA from cells of one or more eukaryotic organisms known to have said disease or condition or a stage thereof, wherein said cells are obtained from, and originate from, a part of said organism distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA; and
- (b) hybridizing the resulting isolated mRNA or isolated cDNA of step (a) to the isolated selected mRNA species or isolated selected cDNA species which are immobilized in the gene transcript pattern probe kit of Claim 53, and assessing the amount of hybridisation so as to obtain said standard gene transcript pattern, wherein the isolated selected mRNA species or isolated selected cDNA species are specific for said disease or condition or stage thereof.

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SUPPLEMENTAL AMENDMENT
CPA of USSN 09/429,003

Claim 58. A method of preparing a test gene transcript pattern for a disease or condition or stage thereof comprising the steps of:

- (a) isolating mRNA from cells of a test eukaryotic organism, wherein said cells are obtained from, and originate from, a part of said organism distant to the area of said disease, wherein the resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA; and
- (b) hybridizing the resulting isolated mRNA or isolated cDNA of step (a) to the isolated selected mRNA species or isolated selected cDNA species which are immobilized in the gene transcript pattern probe kit of Claim 53, and assessing the amount of hybridization so as to obtain said test gene transcript pattern, wherein the isolated selected mRNA species or isolated selected cDNA species are specific for a said disease or condition or stage thereof.

Claim 59. A method of diagnosing or identifying a disease or condition or stage thereof in a test eukaryotic organism comprising the steps of:

- (a) isolating mRNA from cells of a test eukaryotic organism, wherein said cells are obtained from, and originate from, a part of said organism distant to the area of said disease, wherein the

SUPPLEMENTAL AMENDMENT
CPA of USSN 09/429,003

- resulting isolated mRNA is optionally subjected to reverse transcription to obtain isolated cDNA;
- (b) hybridizing the resulting isolated mRNA or isolated cDNA of step (a) to the isolated selected mRNA species or isolated selected cDNA species which are immobilized in the gene transcript pattern probe kit of Claim 53, and assessing the amount of hybridization so as to obtain a hybridization pattern, wherein the isolated selected mRNA species or isolated selected cDNA species are specific for said disease or condition or stage thereof; and
- (c) comparing the resulting hybridization pattern obtained in step (b) with a hybridization pattern obtained by hybridizing isolated mRNA or isolated cDNA prepared from corresponding cells from one or more corresponding eukaryotic organisms known to have said disease or condition or stage thereof to the isolated selected mRNA species or isolated selected cDNA species which are immobilized in said gene transcript pattern probe kit and assessing the amount of hybridization, so as to determine the degree of correlation indicative of the presence of said disease or condition or stage thereof, and so as to diagnose or identify said disease or condition or a stage thereof in said test eukaryotic organism.